WORLD INTELLECTUAL PROPERTY ORGANIZATION. International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C07D 309/32, 405/12, C07C 49/255, 49/577, 49/83, 205/45, 69/734, 69/732, 69/738, 381/04, A61K 31/35

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60/029,906 08/883,743 1 November 1996 (01.11.96) US 27 June 1997 (27.06.97) US

US): (71) Applicant (for all designated States WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BOYER, Frederick, Earl, Jr. [US/US]; 1624 Ironwood Drive, Canton Township, MI 48188 (US). DOMAGALA, John, Michael [US/US]; 47693 Red Run, Canton, MI 48187 (US). ELLSWORTH, Edmund, Lee [US/US]; 6899 Kestrel Court, Brighton, MI 48116 (US). GAJDA, Christopher, Andrew [CA/US]; 2684 Bellwood, Ann Arbor, MI 48104 (US). HAGEN, Susan, Elizabeth [US/US]; 1035 Paddington Road, Canton Township, MI 48187 (US). HAMILTON, Harriet, Wall [US/US]; 204 Jefferson Street, Chelsea, MI 48118 (US). MARKOSKI, Larry, James [US/US]; Apartment 2A, 4920 Lakeridge Drive, Ypsilanti, MI 48197 (US). PRASAD, Josyula, Venkata, Nagendra, Vara [IN/US]; 3129 Fawnmeadow Court, Ann Arbor, MI 48105 (US). TAIT, Bradle, Dean [US/US]; 8431 Congress Drive, Canton, MI 48187 (US). LUNNEY, Elizabeth. Ann [US/US]; 619 Ridgewood Court, Ann Arbor, MI 48103

(74) Agents: RYAN, M. Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.

(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 27 August 1998 (27.08.98)

(54) Title: DIHYDROPYRONES WITH IMPROVED ANTIVIRAL ACTIVITY

(57) Abstract

This invention pertains to improved antiviral activity of 6,6-disubstituted-5,6-dihydropyran-2-ones caused by judicious placement of certain polar substituents at the 3 and/or 6 positions. The same substituents which enhance the cellular activity also diminish cytotoxicity further enhancing the desirable properties of these agents as antivirals.

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Inte onal Application No PCT/US 97/19853

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D309/32 C07D405/12 C07C49/255 C07C49/577 C07C49/83
C07C205/45 C07C69/734 C07C69/732 C07C69/738 C07C381/04
A61K31/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07D A61K C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 125, no. 23, 1996 Columbus, Ohio, US; abstract no. 295892r, P.TUMMINO ET AL.: "discovery a.optimization of non-peptide hiv-1 protease inhibitors." page 459; XP002056515	1,2,14, 16
X	see abstract & BIOORG. MED. CHEM., vol. 4, no. 9, 1996, USA, pages 1401-1410,	1,2,14, 16
X	WO 95 30670 A (UPJOHN) 16 November 1995 see page 88 - page 100; claims; example XXX1; table D1	1,2,14, 16,20

Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance.	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document but published on or after the International filling date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publicationdate of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filling date but later than the priority date claimed	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 16 June 1998	Date of mailing of the international search report 3 0. 06. 98
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Francois, J

Patent family members are listed in annex.

Further documents are listed in the continuation of box C.

onal Application No PCT/US 97/19853

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C07D309/32 C07D405/12 C07C49/255 C07C205/45 C07C69/734

C07C49/577 C07C69/732 C07C69/738 C07C49/83 C07C381/04

A61K31/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07D A61K C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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X	see abstract & BIOORG. MED. CHEM., vol. 4, no. 9, 1996, USA, pages 1401-1410,	1,2,14, 16
X	WO 95 30670 A (UPJOHN) 16 November 1995 see page 88 - page 100; claims; example XXX1; table D1 -/	1,2,14, 16,20

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filling date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filling date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention carnot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention carnot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "8" document member of the same patent family
Date of the actual completion of the international search 16 June 1998	Date of mailing of the international search report 3 0. 06. 98
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016	Authorized officer Francois, J

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Inte ional Application No
PCT-/US 97/19853

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	_
Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 14012 A (PARKE DAVIS) 26 May 1995 cited in the application see claims; example 85	1,2,14, 16,20
Α	WO 95 14011 A (PARKE DAVIS) 26 May 1995	1,2,14, 16
	see claims 7-12	
X	CHEMICAL ABSTRACTS, vol. 100, no. 12, 1984 Columbus, Ohio, US; abstract no. 94556u, page 570; column 1; XP002068172 see abstract & JP 57 167 296 A (RIOCH) 15 October 1982	17
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Inte Ional Application No PCT-/US 97/19853

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In. national application No.

PCT/US 97/19853

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claim(s) 22-26 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows: 1. Claims 1-16, 20 (part.), 22-27 2. Claims 17 3. Claims 18 and 19
4. Claims 21 1. X As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.: Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

In. national application No.

PCT/US 97/19853

Boxi	Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claim(s) 22-26 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
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2. 3.	. Claims 1-16, 20 (part.), 22-27 . Claims 17 . Claims 18 and 19 . Claims 21
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Remai	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Information on patent family members

Inte onal Application No PCT/US 97/19853

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